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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,795	02/22/2002	Fredrik Kamme	PRI-0021 (ORT-1508)	9944

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WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE, 46TH FLOOR
1650 MARKET STREET
PHILADELPHIA, PA 19103

EXAMINER

KIM, YOUNG J

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 12/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/080,795

Applicant(s)

KAMME ET AL.

Examiner

Young J. Kim

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,5,7-14 and 16-23 is/are rejected.
- 7) ☒ Claim(s) 1,3,6,14 and 15 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

This Office Action responds the Appeal Brief received on September 1, 2004.

Upon careful reconsideration of the instant application and the arguments presented in the Brief received on September 1, 2004, the prosecution is hereby reopened.

Preliminary Remark

All objections/rejections hereto not reiterated should be considered withdrawn.

Claim Objections

Claims 1 and 14 are objected to for the following reasons. Instant claims recite that a first strand DNA is synthesized by contacting an mRNA with a reverse transcriptase and that the second strand DNA is synthesized by contacting said first strand DNA with a thermostable polymerase. The art recognized term for such DNA is cDNA. The term DNA embraces genomic DNA (or gDNA) which cannot be made by the recited steps of the claims. It is a well-established fact that mRNA molecules do not contain information from the intronic regions of a genomic DNA. Therefore, when mRNA is reverse transcribed to a DNA molecule, the resulting molecule does not contain the intronic regions of the genomic DNA.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1637

Claims 13, 14, 20, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is indefinite for referring to step (d) in its parent claim 1. Parent claim 1, however, does not have step (d), resulting in insufficient antecedent basis for this limitation in the claim.

Claim 14 is indefinite for the recitation of step (f). Step (f) recites that cRNA produced in step (e) is labeled with a *second* label. However, step (e) already produces a second cRNA which contains a *first* label (from step (d)), resulting in the confusion as to whether the second cRNA contains two labels, or only a single label.

Claims 20 and 21 recite the term, "the array." There is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4, 5, 7-14, and 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mack et al. (U.S. Patent No. 6,566,502 B1, issued May 20, 2003, filed June 30, 2000) in view of Gu et al. (U.S. Patent No. 6,436,677 B1, issued August 20, 2002, filed March 2, 2000).

Art Unit: 1637

Mack et al. disclose a method of producing cRNA from samples, said method comprising the steps of:

- (a) synthesizing a first strand cDNA from total RNA or polyA+ mRNA by contacting said RNA or polyA+ mRNA with T7-T24 oligo (or a first primer) and SuperScript™ RT (or reverse transcriptase) (column 44, lines 33-41);
- (b) synthesizing a second strand cDNA via contacting the synthesized first cDNA strand with *E. coli* DNA polymerase and RNase H (column 44, lines 42-54); and
- (c) In vitro Transcription (IVT) of cDNA into cRNA by contacting the synthesized double stranded cDNA with a T7 RNA polymerase (column 45, lines 1-16).

Mack et al., in producing a second cDNA strand, do not employ the polymerase recited in instant claim 1 (b).

Gu et al. disclose a method of synthesizing a second strand cDNA via use of thermostable polymerases, specifically, Tvu and Bst polymerase (column 29, lines 30-38 and 54-57). The artisans explicitly state that while using the above thermostable polymerase, temperature ranges of 60°-70°C, 60°-75°C, or 50°-75°C are used (column 29).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute a well-known DNA polymerase for the second strand cDNA synthesis, as evidenced by Gu et al. with the DNA polymerase employed by Mack et al. to arrive at the claimed invention for the following reasons.

All of the steps claimed by the instant claim are disclosed by Mack et al., excepting that the polymerase used for second strand cDNA synthesis is an *E. coli* DNA polymerase. However, the use of other well-known DNA polymerase, including such as Bst DNA polymerase, would

Art Unit: 1637

have been well-within the purview of an ordinarily skilled artisan as Gu et al. clearly disclose the use of Bst and other DNA polymerase for generating a second strand of cDNA. MPEP 2143.02, in discussing obviousness, states that the prior art can be modified or combined to reject claims as obvious as long as there is a reasonable expectation of success. Given the teachings of Gu et al. who explicitly states that Bst DNA polymerase, it is clear that one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at substituting the DNA polymerase employed by Mack et al. with any of the well-known DNA polymerase, including Bst DNA polymerase, to arrive at the claimed invention.

With regard to the claimed incubation temperature as being 55°C to 70°C and the incubation time, not only do Mack et al. teach an incubation temperature overlapping this temperature range, but MPEP 2144.05(II), in discussing "obviousness of ranges," states that an optimization through routine experimentation, in the absence of evidence that such claimed range is critical, is obvious.

"A. Optimization Within Prior Art Conditions or Through Routine Experimentation
Generally, *differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical.*" [W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.");< ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons,

Art Unit: 1637

there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)."

Hence, it would have been well-within the purview of an ordinarily skilled artisan at the time the invention was made to be motivated to determine the optimum incubation condition, *i.e.*, temperature and the incubation time, through routine optimization, provided by Gu et al. disclose the use of Bst DNA polymerase in the second strand cDNA synthesis, hence arriving at the claimed invention.

With regard to the labeling of the transcribed cRNA with labels, Mack et al. employs labeled Bio-11-UTP and Bio-16-CTP (column 45, lines 11-13).

The labeled cRNA are hybridized on an array of nucleic acid probes to determine the differential expression of CZA8 (column 48) in tumorous and normal samples (column 59, claim 1).

While Mack et al. are not explicit in disclosing how many polynucleotides probes are immobilized on their array, Mack et al. disclose that known commercial arrays could be used in their method, including Affymetrix GeneChipTM (column 26, line 26), which is known in the art to comprise over 1,000 probes. According to *In re Best* 195 USPQ 430, 1997, the court stated that, "Patent Office can require applicant to prove that prior art products do not necessarily or inherently possess characteristics of his claimed product wherein claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes; burden of proof is on applicant" (pp. 430). Absent evidence to the contrary, the density of the array claimed by the instant application is determined to be met by Mack et al.

Art Unit: 1637

With regard to the use of Cy₃ and Cy₅ for differential labeling, Mack et al. states that the nucleic acids could be labeled with Cy₃ or Cy₅ (column 17, lines 16-20; column 31, lines 40-43).

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

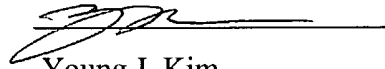
The prior art does not teach or suggest a method of synthesizing a second strand cDNA using a thermostable polymerase, wherein said thermostable polymerase is a Bst large fragment polymerase, which is different from the native Bst polymerase in that it lacks a 5'-3' exonuclease domain (page 190, 2nd column, bottom paragraph, *Aliotta et al.*) (Aliotta et al., Genetic Analysis Biomolecular Engineering, 1996, vol. 12, no. 5-6, pages 185-195).

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner can normally be reached from 8:30 a.m. to 6:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a

Art Unit: 1637

general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.



Young J. Kim
Patent Examiner
Art Unit 1637
12/1/04

YOUNG J. KIM
PATENT EXAMINER

yjk



GARY BENZION, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600